Reliability of sleep deprivation-associated spontaneous brain activity and behavior

Lei Gao[1,2†], Lijun Bai[3†], Yuchen Zhang[4], Xi-jian Dai[2], Rana Netra[1], Youjiang Min[5], Fuqing Zhou[2], Honghan Gong[2*], Ming Zhang[1*], and Yijun Liu[6,7]

1. Department of Medical Imaging, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China
2. Department of Radiology, the First Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi Province, China
3.The Key Laboratory of Biomedical Information Engineering, Ministry of Education, Department of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an 710049, China
4. Zonglian Experimental Class, Xi'an Jiaotong University, Xi'an 710049, China
5. Acupuncture & Rehabilitation Department, Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang 330006, Jiangxi Province, China
6. Southwest University, School of Psychology, Key Laboratory of Cognition and Personality, Chongqing, Chongqing 400715, China
7. Departments of Psychiatry and Neuroscience, McKnight Brain Institute, University of Florida, Gainesville, FL 32610, USA.

* Correspondence to Honghan Gong, Department of Radiology at the First Affiliated Hospital of Nanchang University, 17 Yongwaizheng Ave., Nanchang 330006, Jiangxi Province, China
Email:honghan_gong@sina.com (Hong-Han Gong);
and Ming Zhang, Department of Medical Imaging at the First Affiliated Hospital of Xi'an Jiaotong University, 277 West Yanta Road, Xi'an 710061, Shaanxi Province, China. Email: zmmri@163.com (Ming Zhang)
† Contribute equally to this paper.

Abstract

Recent studies have indicated that sleep deprivation (SD) alters intrinsic low-frequency connectivity in the resting brain, mainly focusing on the default mode network (DMN) and its anticorrelated network (ACN). These networks hold key functions in segregating internally and externally directed awareness. However, far less attention has been paid to investigation of the altered amplitude of these low-frequency fluctuations (ALFF) at the whole-brain level and more importantly by what extent the sleep-deprived resting brain pattern can be reproducible and predict individual behavioral performance. The aim of this study was to characterize more clearly the influence of sleep on the whole brain level of ALFF changes and its relation with the performance of a lexical decision task in the sleep deprivation. Sixteen healthy participants underwent fMRI three times: once after a normal night of sleep in the rested wakefulness (RW) state and two following approximately 24 h of total SD separated by an interval of two weeks (SD1 and SD2). Our behavioral results showed that sleep stabilizes performance whereas two sleep deprivation even at an interval of two weeks consistently deteriorates it. Sleep deprivation attenuated the ALFF mainly in the bilateral orbitofrontal cortex (OFC), bilateral dorsolateral prefrontal cortex (DLPFC) and right inferior parietal lobule (IPL). By contrast, the enhanced ALFF emerged in the left sensorimotor cortex (SMA), visual cortex and left fusiform gyrus. Conjunction analysis of SD1 and SD2 versus the control maps and voxel-wise ICC analysis revealed that these SD induced ALFF changes showed a significantly high reliability (ICC＞0.5). Particularly, the attenuation of the right IPL presents a significant negative relation with the behavior performance and can be reproducible for two SD at an interval of two weeks. Our results suggest that ALFF is a stable measure in study of SD, and the right IPL may represent a stable biomarker that responds to sleep loss.

Keywords: sleep deprivation, resting-state fMRI, ALFF, test-retest, reliability

Introduction

Sleep deprivation (SD) repeatedly show a variable (negative) impact on mood, cognitive performance, and motor function due to increasing sleep propensity and destabilization of the wake state (Goel et al., 2009). Previous neuroimaging studies have shown that insufficient sleep can have a number of adverse effects on brain functioning. The investigation of the neural mechanism underlying SD by using fMRI is still in the initial stage, but has already provided a wealth of information about sleep-deprived brain networks and various functions that support normal waking behavior. Various neuroimaging studies have found altered activation patterns of sleep-deprived brain during a number of tasks including memory (Chee and Choo, 2004; Chee et al., 2006; Mu et al., 2005; Mu et al., 2005; Sterpenich et al., 2009; Van Dongen, 2005), attention (Chee and Tan, 2010; Chee et al., 2008; Kong et al., 2012), executive functioning (Drummond and Brown, 2001; Muto et al., 2012), and decision making (Chee et al., 2010; Kong et al., 2011; Libedinsky et al., 2011). Several brain regions, such as the prefrontal cortex, parietal cortex, sensorimotor area, visual cortex, thalamus and cingulate cortex have been frequently reported to be associated with SD.

Prolonged wakefulness has been associated with altered functional integrations in the resting brain. The default mode network (DMN), with a relatively high rCBF (Gusnard et al., 2001; Raichle et al., 2001) and a high level of correlated BOLD signal fluctuations (Greicius et al., 2003; Raichle, 2011) at rest, is considered to support self-awareness (Gusnard et al., 2001) and conscious self-representation (Lou et al., 2004). Investigations of the influence of SD on the DMN had shown significantly disrupted deactivations and led to double dissociations within anterior as well as posterior midline regions of the DMN (Gujar et al., 2010). This finding invites the speculation that the decreased DMN connectivity could be intrinsic to the sleep deprivation or a reflection of changes in vigilance (De Havas et al., 2012; Samann et al., 2010). In addition, the DMN is anticorrelated with the cognitive control network (CCN), a corresponding task-positive network, which encompasses bilateral fronto-cingulo-parietal structures including lateral prefrontal and superior parietal areas (Niendam et al., 2012). Abnormal connectivity within DMN and its anticorrelated networks (CCN) have also been reduced after SD (Bosch et al., 2013; De Havas et al., 2012; Samann et al., 2010; Shao et al., 2013). DMN-CCN interactions

may be considered to reflect the level of consciousness that is required for information integration (Heine et al., 2012; Larson-Prior et al., 2011). More recently, two studies pointed out that enhanced functional connectivity between the dorsal nexus and dorsolateral prefrontal cortex, as well as attenuated functional connectivity within thalamocortical, also occurrs after a SD (Bosch et al., 2013; Shao et al., 2013). These findings indicate disrupted temporal synchronization of the global resting-state network in the sleep-deprived brain. However, these investigations generally adopted the seed-based functional connectivity method and did not allow for a direct assessment of regional activity during the resting brain. In other words, abnormal functional interactions between two remote areas cannot address the question on which area is responsible for such observable connectivity alternations.

In light of this view, we aimed to measure the amplitude of low-frequency fluctuation (ALFF) in sleep-deprived resting brain. ALFF, without a priori selection of regions of interest, can be used to study the dynamics of the BOLD signal at the local, voxel-wise level, without assessing the relationship between regions (Zang et al., 2007). In addition, such method has proven to be test-retest reliability across time (Li et al., 2012; Turner et al., 2012; Yan et al., 2013; Zuo et al., 2010), and can successfully predict magnitudes of the task-evoked activity (Mennes et al., 2011; Zou et al., 2013). The present study attempted to address the following issues: *i)* by which way sleep-deprived brain reflects abnormal patterns of ALFF; *ii)* whether such patterns are reproducible over a two-week interval SD; *iii)* to what extent the inter-subject differences in the ALFF resting activity may predict individual behavioral performance. For this purpose, a lexical decision task was also used as a paradigm to test the effects of sleep loss and fatigue on the dynamic time-course of responses to cognitive load (Babkoff et al., 1985; Forster and Forster, 2003; L O Pez Zunini et al., 2014).

Materials and Methods

Subjects

Sixteen healthy volunteers (8 females, mean age of 22.1 ±0.8 years) were recruited in this study after giving the informed consent. Participants were selected from respondents to a web-based questionnaire. They should meet the following criteria: (1) right-handed according to

the modified Edinburgh Handedness Questionnaire (Oldfield, 1971); (2) between 20 and 24 years of age; (3) good sleeping habits (sleeping no less than 6.5 h each night for the past one month); (4) not be of extreme morning or evening chronotype (score no greater than 22 on a modified Morningness–Eveningness scale; Horne and Ostberg, 1976); (5) no long-term medications; (6) no symptoms associated with sleep disorders; (7) no history of any psychiatric or neurologic disorders; (8) no history of drug abuse and current use of anti-depressant or hypnotic medications. Participants had an average of 15.7 ± 1.2 years of education. This study was approved by the medical research ethics committee and institutional review board of The First Affiliated Hospital of Nanchang University.

Participants showed normal sleep quality as assessed using the Pittsburgh Sleep Quality Index (PSQI) [37] (mean ±SD, 1.5 ±0.97) and normal daytime sleepiness as assessed using the Epworth Sleepiness Scale (ESS)[38] (mean ±SD, 6.44 ±2.07). They had a BMI (in kg/m^2) of 17.5–22, and were free of nightshift work. Before experiment (approximately 4 weeks before), subjects were required to sleep 7–9 h/night, preceding 00:10 a.m on average and keep sleep logs.

Sleep deprivation and experimental protocol

All subjects were scheduled for three fMRI scans starting at 7:00 PM. One scan follows the individual's normal sleep (RW group), while the other two after a night of total SD (i.e., SD1 and SD2 groups). Two SD sessions were approximately two weeks apart. The sequence of experiments was counterbalanced across sessions and approximately two weeks apart between two experiments. This was to ensure minimizing the possibility of residual effects of SD on cognition in participants whose SD session preceded their rested wakefulness session. Subjects were forbidden to tea, coffee or caffeine content drinks and alcohol intake for 72 h before fMRI examinations. Sleep logs were kept for a week prior to the study night. During SD, subjects were monitored in the lab onward and only allowed to engage in non-strenuous activities such as reading and watching videos. Vigorous physical activity prior to the scans was forbidden.

A behavior test was performed for each subject prior to fMRI scanning. Word stimuli were displayed using the experimental software DMDX v.3.0.4 (Forster and Forster, 2003). White-color words of 10 mm in size were presented on monitor with a black background in a

dimly lit room. During the experiment, each pair of stimuli was presented for 900 ms separated by a blank screen for 500 ms. Subjects had 2,500 ms between trials to judge whether the two words were semantically related or not. A positive response was indicated by pressing the right button using the middle finger of the right hand, while a negative response was represented corresponding left button to the index finger of the right hand. Participants were encouraged to proceed as quickly and accurately as possible. Accuracy and reaction times (RTs) (to the nearest millisecond) were recorded. Before the formal test, a short period of practice with a different set of sentences was provided.

Data acquisition

fMRI data were collected on a SIEMENS Trio 3.0 T scanner. Each subject lied on supine with the head in neutral position fixed comfortably by a belt and foam pads during the test. The scanning sessions included: (1) localizer, (2) T1 MPRAGE anatomy (176 sagittal slices, thickness/gap = 1.0/0 mm, in-plane resolution = 256 × 256, FOV (field of view) = 240 mm × 240 mm, TR (repetition time) = 1,900 ms, TE (echo time) = 2.26 ms, flip angle = 15 °), (3) EPI-BOLD (36 axial slices, echo-planar imaging pulse sequence, thickness/gap = 5.0/1 mm, in-plane resolution = 64 × 64, TR = 3,000 ms, TE = 30 ms, flip angle = 90 °, FOV = 240 mm × 240 mm). During the resting-state fMRI session, subjects were required to be as calm as possible, to keep their eyes closed but not to fall asleep to ensure a successful image acquisition.

Behavioral analysis

To examine changes in behavior performance over the course of the SD sessions, the mean RT and false rates (button pressed following a cue) to measure the accuracy of performance were computed respectively.

Data preprocessing

All preprocessing was performed using the Data Processing Assistant for Resting-State fMRI (DPARSF, Yan and Zang, 2010, http://www.restfmri.net), which is based on Statistical Parametric Mapping (SPM8) (http://www.fil.ion.ucl.ac.uk/spm) and Resting-State fMRI Data Analysis Toolkit (REST, Song et al., 2011, http://www.restfmri.net). For the resting-state fMRI

data on each subject, the first two volumes were discarded to avoid the possible effects of scanner instability and adaptation of subjects to the circumstances.

The following sequence of preprocessing steps was performed: *i)* slice timing (correction for the within-scan acquisition time differences between slices); *ii)* head motion correction (realignment and a six-parameter spatial transformation). Recent studies indicate that head motion can significantly influence measures and results derived from the resting-state fMRI(Power et al., 2012; Van Dijk et al., 2012; Yan et al., 2013), we computed the voxel-specific head motion, including voxel-specific framewise displacement (FD_{vox}) and voxel-specific total displacement (TD_{vox}) values for each subjects by using the DPARSF toolbox. Group differences of mean FD_{vox} were calculated by using two-sample t-test while with no significant group differences. Then the mean FD was used as a covariate in the group comparisons of ALFF. In our study, absolute head movement was below 0.5 mm and 0.5 °for all subjects; *iii)* spatial normalization to the Montreal Neurological Institute (MNI) template (resampling voxel size = 3×3×3 mm^3); *iv)* spatial smoothing (full width at half maximum (FWHM) = 6 mm Gaussian kernal);*v)* linear detrend and voxel-wise bandpass filtering (0.01 - 0.08 Hz).

For ALFF analysis, for a given voxel, the time series was first converted to the frequency domain (0.01-0.1Hz) using a Fast Fourier Transform (FFT). The square root of the power spectrum was computed and then averaged across a predefined frequency interval. This averaged square root was termed ALFF at the given voxel. ALFF measures the absolute strength or intensity of LFF. ALFF of each voxel was computed for each participant and was further divided by the global mean value to reduce the global effect of variability across participants.

Test-retest reliability analyses

Test-retest reliable measurements are important for the inference of convincing conclusions. To investigate the test-retest reliability of SD, we further calculated voxel-wise intraclass correlation coefficients (ICC) between two SD sessions (Zuo et al., 2010).

Statistical analyses

We used paired *t*-test for SD vs. RW groups to determine the effects of SD on performance measures of RT. For ALFF, a one-sample one-sided *t*-test was performed inter-group to determine whether the ALFF differed from 1 (Raichle et al., 2001; Zang et al., 2007), and a paired *t*-test to see the differences between groups. Voxels with a p value < 0.01, cluster size > 1,053 mm^3 (39 voxels) were considered to be a significant statistical difference between two groups, which also corresponds to a multiple corrected p<0.05 in the AlphaSim program (http://afni.nih.gov/afni/docpdf/AlphaSim.pdf).

Conjunction analysis

A conjunction of SD1 and SD2 versus control maps was calculated to determine brain areas that commonly and similarly differently in both SD1 and SD2.

Brain–behavior relationships

To further evaluate the relationship between ALFF changes and behavioral performance after SD, we examined the Pearson's correlation between the mean ALFF values of peak voxels of areas derived from the inter-group comparison and behavioral performance of RT.

Results

Performance findings

There were no significant differences in the accuracy rate between the SD and RW groups. The two SD groups had significantly longer reaction time than that of the RW group (RW = 2,010.4 ±227.17 (ms), SD1 = 2,275.1 ±176.66 (ms), T = -3.858, d.f. = 15, P < 0.002; SD2 = 2,172.2 ± 166.51 (ms), T = -2.584, p < 0.021) (Fig. 1).

ALFF differences in two SD sessions

Comparing with the RW group, both SD groups showed the decreases of ALFF mainly in the bilateral orbitofrontal cortex (OFC) (BA 11/47), bilateral dorsolateral prefrontal cortex (DLPFC) (BA 46) and right inferior parietal lobule (IPL, BA39/40), while the increases of ALFF

emerged primarily in the somatosensory cortex (SMC), fusiform gyrus (BA 37) and middle occipital gyrus (MOG) (BA 18/19) (Fig. 2 and Table.1).

Conjunction analysis and voxel-wise ICC analysis

The overlap of SD1 and SD2, compared to control group, shared the same areas primarily in the Pcu/PCC, OFC, SMC, bilateral occipital cortex, and right IPL (shown in Fig. 3.). The high reliability derived from the intra-subject test-retest analysis existed in most of brain areas (ICC $\geqslant$0.5, Fig.3). These areas mainly located at the precuneus /PCC, cingulate cortex, bilateral SMC, bilateral parietal cortex, bilateral MPFC, and bilateral occipital cortex.

Correlations between ALFF and behavior performance in the SD group

In this study, the greater the prolongations in the RT from rest to SD, the greater the decrease in ALFF in the right IPL reproducible by two SD at an interval of two weeks (for SD1, r = -0.561, $p < 0.024$; while for SD2, r = -0.499, $p < 0.05$) (Fig.4).

Discussion

Several observations emerged from the examination of spontaneous "low frequency" fluctuation from temporal synchronization (i.e. functional connectivity) in sleep-deprived resting brain. Beyond verifying the altered intrinsic patterns in "off-line" brain, we noted that even one night of sleep loss can alter the ALFF, especially attenuations in the bilateral OFC, bilateral DLPFC, and right IPL, while enhancements in the SMC, thalamus, fusiform gyrus and visual cortices. Moreover, the measurements of the ALFF patterns in the sleep-deprived brain are quite reliable over time with an interval of two weeks. These relatively high stability coefficients provided conservative estimates of the test-retest reliability of ALFF in SD. In addition, the inter-subject differences in ALFF measures provide a clue to predict the individual behavioral performance, which showed a significantly negative relation of RT with the ALFF of the right IPL.

Significantly different patterns of ALFF were found between SD and RW. Consistent with previous task-evoked activations in varied cognitive stimuli, our findings showed that altered

ALFF changes were mainly located in the DLPFC, OFC and IPL. It is believed that the frontal-parietal areas are particularly vulnerable to SD (Bosch et al., 2013; Chee and Tan, 2010; Chuah et al., 2010; Lythe et al., 2012). Decreased activities in the prefrontal and parietal were especially found in several working memory studies, therefore parietal activity represents a biomarker of individual response to sleep debt (De Havas et al., 2012). Inadequate sleep is also associated with exaggerated emotional responses (Chuah et al., 2010; Goldstein et al., 2013; Killgore, 2013; Menz et al., 2012; Minkel et al., 2012; Mullin et al., 2013). The OFC, known as the limbic system, is thought to be critical for mediating the interactions between emotional processes and cognitive functions, such as decision making (Azzi et al., 2012; Kahnt et al., 2012; Parsons et al., 2013; Zald et al., 2012). We speculate that SD may influence emotion and cognition regulation circuitry, and lead to deficient capacity to regulate emotional arousal and cognitive loads.

Besides impairments in sleep-deprived resting brain, it was also worthy to note that enhanced ALFF mainly emerged in the SMC, fusiform gyrus and visual cortex, which may reflect compensation mechanism after sleep loss, and an attempt to maintain hyperarousal. Early PET and fMRI studies investigate brain responses to attention tasks following SD, and also find such hypermetabolism in the visual cortex and sensorimotor areas (Thomas et al., 2000). They inferred that such an enhancement of brain activity might indicate a homeostatic drive for recovery of brain areas involved in attention and higher-order cognitive processes, interpreted as compensatory mechanisms to maintain alertness and cognitive performance in the face of extended wakefulness. A recent study of enhanced functional connectivity between primary sensory processing and motor planning regions in insomnia provides further evidence, consistent with our results (Killgore et al., 2013). This may imply ALFF encodes tendency for task response even during the resting state.

As expected, we found highly reproducible ALFF patterns at a two-week interval in the sleep-deprived brain. The overlapped areas presented in our study included the PCC, OFC, IPL, SMC, visual cortex and right insula via the conjunction analysis. Voxel-wise ICC map showed the spatial distribution of the reliability of the observed ALFF, mainly along the midline

structure of the brain, lateral prefrontal and parietal cortex ($p < 0.001$). This finding was in line with previous task-fMRI research (Lim et al., 2007), which has shown reproducible brain activations highly correlated across sessions in a frontoparietal network during a working memory task. As in previous studies, stable drop in the left parietal activation over time, we denoted that these tasks-evoked brain activity and behavior changes may underlie intrinsic brain activity. The reliability of the resting spontaneous activity pattern, acting as a functional framework for a moment-to-moment responses, remains uncovered. In the present study, we confirmed its stability over a two-week interval. Along the same lines, some studies also found reliability of the ALFF in chronic schizophrenia (Turner et al., 2012) and healthy state (Li et al., 2012) during a short period of time. This may support the notion that, in a relatively short duration, intra-individual resting dynamics to SD load stably exists.

At resting state, the brain featured by exhibiting an intrinsic organization that includes both "task-negative" (DMN) and its anticorrelated "task-positive" networks (ACN) (Fox et al., 2005). DMN characterized by more energetic metabolic and neural activity at rest engaged in internally focused tasks, such as autobiographical memory retrieval, implicit learning, prospection, monitoring and other internally focused thought processes (Braga et al., 2013; Raichle et al., 2001; Uddin et al., 2009). Decreased ALFF signals in the PCC, bilateral OFC (BA 11/47) and right inferior parietal lobule (IPL, BA39/40) following 24h SD may be associated with maladaptive ability to switch the default mode activity when task conditions required attentions. The DLPFC, one of the "task-positive" regions (ACN) , has been implicated to be responsible for the failure in working memory in SD (Goel et al., 2009). In our study, reduced DLPFC activity may suggest dysfunctional integrations between the DMN and ACN, and this is consistent with reduced anti-correlation between DMN and ACN nodes during both task and resting states (De Havas et al., 2012). Moreover, the interesting finding is the increased ALFF in the SMC, visual cortex and left FG. According to the sleep homeostatic hypothesis (Born and Feld, 2012; Tononi and Cirelli, 2003, 2006), one possible explanation may be the compensatory reallocates—the resting brain reallocate its oscillatory dynamics resources. This reconfiguration reduces the adaptation of neural resources in response to increased cognitive challenges and emotion regulations.

The results obtain reproducible behavior performance following the SD at an interval of two weeks. Besides the reliability, there is a significant negative linear correlation between the ALFF decrease in the right IPL and RT when performing lexical decision task. Plentiful studies have found that sleep loss can significantly degrade performance on tasks that incorporate a working-memory component or that otherwise are thought to require contributions from frontoparietal cortical regions (Goel et al., 2009). The IPL, as an important association area of integrating sensory information, plays a prominent role in visuospatial attention. Successful performance of the semantic priming tasks demands participants to sustain mental effort, strategically control and quickly focus their attention in order to accurately register transient stimulus events, as well as rapidly compare incoming information to that maintained in working memory. In this study, the significantly negative linear correlation may suggest that spontaneous activity of the IPL was impaired with sleep loss load. Many reports, though some divergent, are associated reduced task-evoked parietal activation with a decline in behavioral performances. One recent study from resting functional connectivity also support the notion that activity changes in the IPL may reflect the early effects of SD (De Havas et al., 2012). Therefore, it is reasonable to suggest that reduced resting state intrinsic activity in the IPL may relate to declining cognitive capacity in SD.

Limitations

There are several limitations in this study. Firstly, a relatively small sample, the statistical power lowers and limited, so the results can hardly survive a strict multiple comparison correction (e.g. FDR or FWE correction). Future studies could use a larger sample size to increase the statistical power of the study. Secondly, a lack of objective assessment of both self-reported sleepiness and mood items. Further investigations should be focused on a more detailed frequency-dependent analysis.

Conclusion

Our high test-retest reliability of ALFF patterns highlighted the notion that sleep burden reshapes the low frequency dynamics in the resting brain, and this sleep-deprived brain pattern

can predict the individual behavior performances. This finding may provide much deeper insights into the understanding of SD related underlying neurological underpinnings of cognitive declines.

Conflict of Interests

There is no competing interest.

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Table 1. Brain areas of ALFF differences between the RW and SD group. Coordinates x, y, z (mm) are given in standard stereotactic MNI space. All regions listed are statistically significant at the $p < 0.05$, AlphaSim corrected. L: left; R: right.

SD1:

Brain regions	MNI coordinates			BA	L/R	Voxels	T values
	x	y	z				
Superior Frontal Gyrus	-12	66	6	10	L	202	-4.27
Middle Frontal Gyrus	45	27	30	46	R	47	-3.62
Middle Frontal Gyrus	-45	39	-6	46/47	L	47	-4.03
Inferior Frontal Gyrus	54	18	0	22/47	R	82	-4.01
Middle Occipital Gyrus	-51	-66	-15	19/37	L	653	4.66
Middle Occipital Gyrus	42	-60	-9	19	R	109	4.35
Middle Occipital Gyrus	-12	-72	0	18/19	L	101	3.99
Thalamus	21	-15	12	-	R	98	4.37
Thalamus	-18	-18	3	-	L	40	4.19
Inferior Parietal Lobule	45	-60	33	39/40	R	148	-5.48
Precuneus/ Posterior Cingulate	3	-63	30	31/7	R	70	-5.58
Precentral Gyrus	-36	-9	60	1/2/3/4/6	L	738	7.32
Precentral Gyrus	-54	-3	36	3/4/6	L	41	4.14

SD2:

Brain regions	MNI coordinates			BA	L/R	Voxels	T values
	x	y	z				
Medial Frontal Gyrus	15	66	-3	11/10	R	54	-5.22
Superior Frontal Gyrus	-42	48	0	10/46	L	39	-4.62
Middle Frontal Gyrus	-51	33	27	9/46	L	40	-5.01
Inferior Frontal Gyrus	-51	36	0	10/47	L	62	-4.62
Insula	-33	-18	21	13	L	378	8.99
Insula	36	-15	21	13	R	56	4.67
Post Cingulate Gyrus	0	-33	33	23/31	L	30	-4.51
Inferior Parietal Lobule	66	-48	24	39/40	R	156	-6.09
Precentral Gyrus	36	-24	36	2/3/4/6	R	319	6.51
Precentral Gyrus	-36	-12	57	1/2/3/4/6	L	652	10.06
Middle Occipital Gyrus	-39	-87	0	18/19	L	413	6.79
Medial Frontal Gyrus	15	66	-3	11/10	R	54	-5.22
Superior Frontal Gyrus	-42	48	0	11/46	L	39	-4.62

Figure Legends

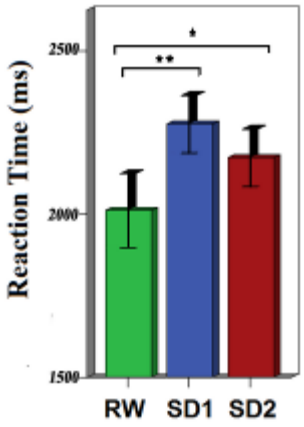


Figure 1. Effects of 24h sleep deprivation on RT for semantic tasks. Y-axes show the mean (±2 sd) time of RT for each group. X-axes indicate the group. Significantly different (*p < 0.05, **p < 0.01) groups are as indicated.

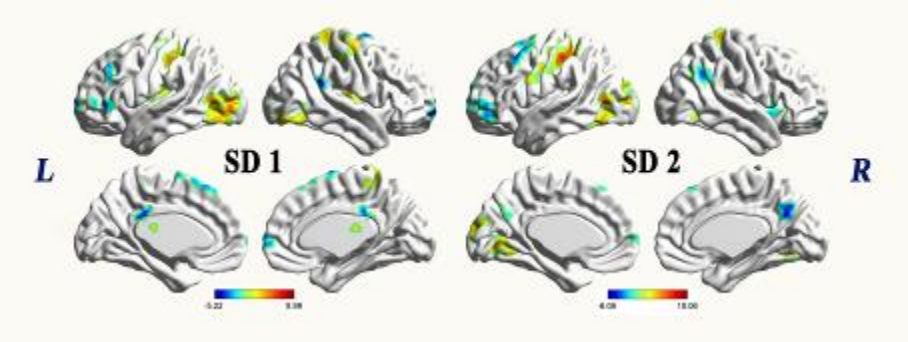
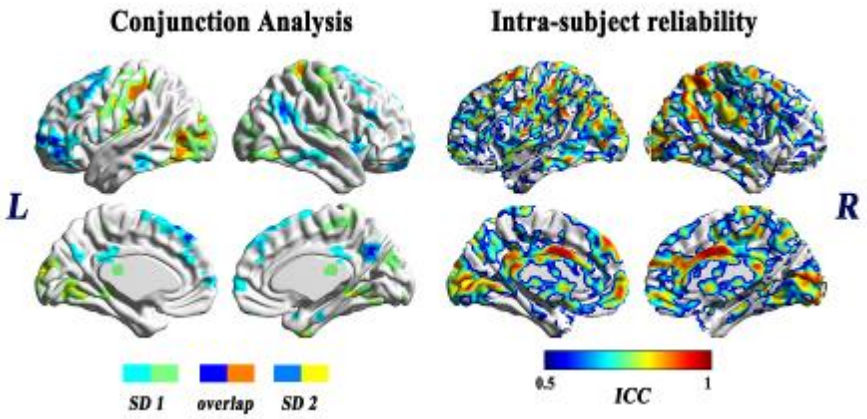


Figure 2: Group ALFF differences in the two SD sessions. The effects are significant at p < 0.05, AlphaSim corrected. Cool color indicates that the SD group had decreased ALFF compared with the controls and the hot color indicates the opposite.The results were visualized with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/).



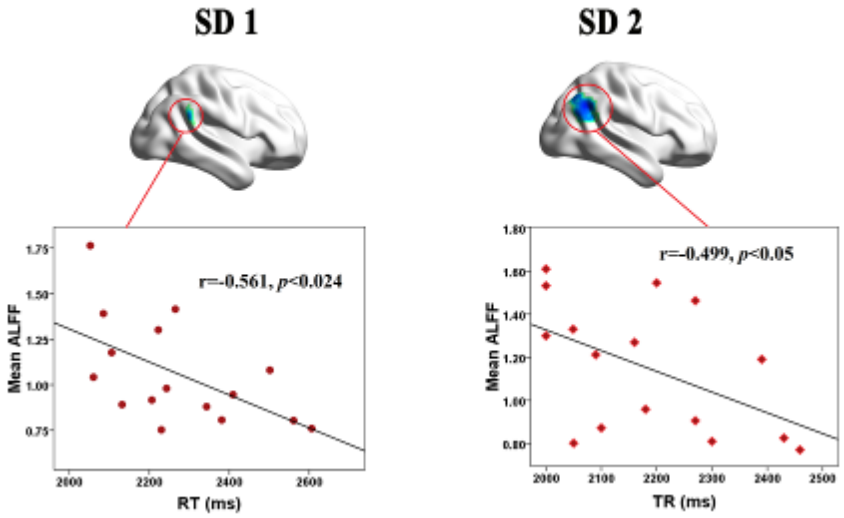
549

550 **Figure 3: Overlap of SD1 and SD2 compared to control differences.** 2 SD sessions shared the

551 same areas are shown in brown and blue. **Voxel-wise ICC.** The intra-subject test-retest reliability

552 for two SD sessions, the regions with high reliability (ICC > 0.5) are shown. The results were

553 visualized with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/).



554

555 **Figure 4**: **The correlation between RTs and ALFF change in the right IPL in the sleep**

556 **deprivation group.** The greater the prolongations in RT from rest to sleep deprivation, the

557 greater the decrease in ALFF in the right IPL. The results were visualized with the BrainNet

558 Viewer (http://www.nitrc.org/projects/bnv/).

559